Genotype-guided strategy for antithrombotic treatment versus conventional clopidogrel therapy in peripheral arterial disease.

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We hypothesize that genotype-guided prescription of antithrombotic treatment reduces adverse clinical events related to arterial thrombosis.

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26517

Bron
Nationaal Trial Register

Verkorte titel
GENPAD

Aandoening

Peripheral arterial disease

Ondersteuning

Primaire sponsor: Radboudumc
Overige ondersteuning: ZonMW ZE&GG

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome is the number of participants that experienced a major adverse cardiovascular events, major adverse limb events or death from any cause during a median follow-up of 24 months.(range 6 to 36 months)

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Peripheral arterial disease (PAD) is a common presentation of atherosclerosis, resulting in intermittent claudication, pain at rest or gangrene. For the prevention of adverse events related to arterial thrombosis in PAD patients, clopidogrel is recommended. Clopidogrel in itself is inactive and needs to be metabolized by cytochrome P450 2C19 (CYP2C19) into the active metabolite. About 30% of PAD patients receiving clopidogrel is carrying one or two CYP2C19 loss-of-function allele(s) and do not or to a limited extent convert the prodrug into its active metabolites, and are therefore at increased risk of adverse clinical events related to arterial thrombosis and subsequent cardiovascular death. We hypothesize that genotype-guided prescription of antithrombotic treatment reduces adverse clinical events related to arterial thrombosis.
Objective: The primary aim of the GENPAD study is to evaluate the ability of genotype-guided antithrombotic treatment to reduce adverse clinical events related to arterial thrombosis in PAD patients. Adverse clinical events of interest are major adverse cardiovascular events (myocardial infarction, stroke, transient ischemic arrack), major adverse limb events (acute/chronic limb ischemia of peripheral vascular intervention including amputation) and death. Secondary objectives are to evaluate the ability of genotype-guided antithrombotic treatment to reduce the separate elements of the primary composite outcome and to assess the risk of clinically relevant bleedings in patients allocated to the genotype-guided antiplatelet treatment versus standard clopidogrel prescription. Other objectives are to evaluate cost-effectiveness, to explore health state scores and health-related quality of life between study groups and metabolizer states and to set-up a biobank.
Study design: A randomized, controlled, open label, multicenter trial.
Study population: Patients (n=2276) with PAD consulting a vascular surgeon for diagnosis and/or treatment, receiving clopidogrel according to the guidelines.
Intervention: Testing for carriage of the CYP2C19*2 and *3 loss-of-function alleles, followed by a genotype guided antithrombotic treatment with either clopidogrel 75mg once daily (normal metabolizers), clopidogrel 75mg twice daily (intermediate metabolizers), or low-dose rivaroxaban plus acetylsalicylic acid (poor metabolizers).
Comparator: All patients receive clopidogrel 75mg once daily without pharmacogenetic guidance.
Main study parameters/endpoints: The primary combined outcome is the occurrence of adverse clinical events related to arterial thrombosis at 24 months. The occurrence of major adverse cardiovascular events, major adverse limb events, death and clinically relevant bleedings are the secondary endpoints. Health state, quality of life and medical consumption will be measured with validated questionnaire. Tailormade questionnaires will be used to assess which antithrombotic treatment the participant is receiving during follow-up,

medication adherence and the occurrence of extramural adverse events at 6, 12, 24 and 36 months.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participants will visit the hospital once for informed consent procedure, blood sample withdrawal and/or buccal sample collection This visit will be combined with a routine visit to the vascular surgeon or vascular laboratory. Patients might experience some discomfort while taking blood samples and buccal sample collection for a short amount of time. The follow-up of participants will range from 6 months (minimum) to 36 months (maximum). Participants are sent questionnaires at baseline and at 6, 12, 24 and 36 months, dependent on the duration of their follow-up. Completing the questionnaires will take approximately 30 minutes. Risks regarding the study are negligible and consist of the possible adverse events related to doubling the daily dose of clopidogrel or related to rivaroxaban and acetylsalicylic acid.

Doel van het onderzoek

We hypothesize that genotype-guided prescription of antithrombotic treatment reduces adverse clinical events related to arterial thrombosis.

Onderzoeksopzet

24 months

Onderzoeksproduct en/of interventie

Testing for carriage of the CYP2C19*2 and *3 loss-of-function alleles, followed by a genotype guided antithrombotic treatment with either clopidogrel 75mg once daily (normal metabolizers), clopidogrel 75mg twice daily (intermediate metabolizers), or low-dose rivaroxaban plus acetylsalicylic acid (poor metabolizers).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Age > 16 years
- Obtained written informed consent
- Indication for monotherapy clopidogrel 75mg once daily
- Ankle-brachial index < 0.9 and/or toe brachial index < 0.5
- Current or previous symptoms due to insufficient vascularization of one or two lower extremities, including intermittent claudication, pain at rest and/or gangrene (Rutherford category 1-6)
- Consulting a vascular surgeon for diagnosis, treatment and/or follow-up of peripheral arterial disease

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- known CYP2C19 genotype or metabolizer state
- treated with coumarins, Non-vitamin K Oral Anti-Coagulants (NOACs), unfractionated heparin (UFH), low molecular weight heparins (LMWH) or double antiplatelet therapy (DAPT) with ASA and a P2Y12 inhibitor for other indications
- contraindication for clopidogrel, ASA and/or rivaroxaban
- pregnant or breastfeeding women
- unable to give informed consent (including not being able to understand the Dutch language)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd

Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-03-2021
Aantal proefpersonen:	2276
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
Data will be accessible through the DANS EASY repository, using Dublin Cor metadata scheme

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 50838
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9027
CCMO	NL75567.091.20

Register	ID
OMON	NL-OMON50838

Resultaten